

FIG. 1. Summary of meningococcal outer membrane vesicle vaccine efficacy trials*

| Years of the Study | Vaccine Strain | Location (population vaccinated) | Age (years) | Estimated Efficacy (%) |
|--------------------|-------------------------|--|----------------------|---------------------------|
| 1987-89 | B:4:P1.15 C PS /alum | Cuba (100,000 school children) | 11 to 16 | 83 |
| 1989-90 | B:4:P1.15 C PSb/alum | Sao Paolo, Brazil (300,000 children) | 2 to 4 4.1 to 7 | 47 74 |
| 1990-91 | B:4:P1.15 C PS/alum | Rio de Janeiro, Brazil (2.4 million children) | 3/12 to 7 4. to 7 | 58 71 |
| 1988-90 | B:4:P1.3 C PS/alum | Iquique, Chile (40,000 children) | 1 to 3.9 4 to 21 | -23 70 |
| 1989-91 | B:15:P1.7,16 alum | Norway (171,800 school children) | 14. to 16 | 57 |

*Adapted from Frasch (1995, in MENINGOCOCCAL DISEASE, K. Cartwright (ed.), Wiley, New York, NY, p. 266). In Norway, two doses of vaccine were given separated by 6 weeks. Efficacy was 87% in the first year and then declined during the subsequent 18 months follow-up, so that overall efficacy was 57%. C PS=Serogroup C polysaccharide vaccine that is mixed with the vesicles. Alum preparations were Al(OH)₃

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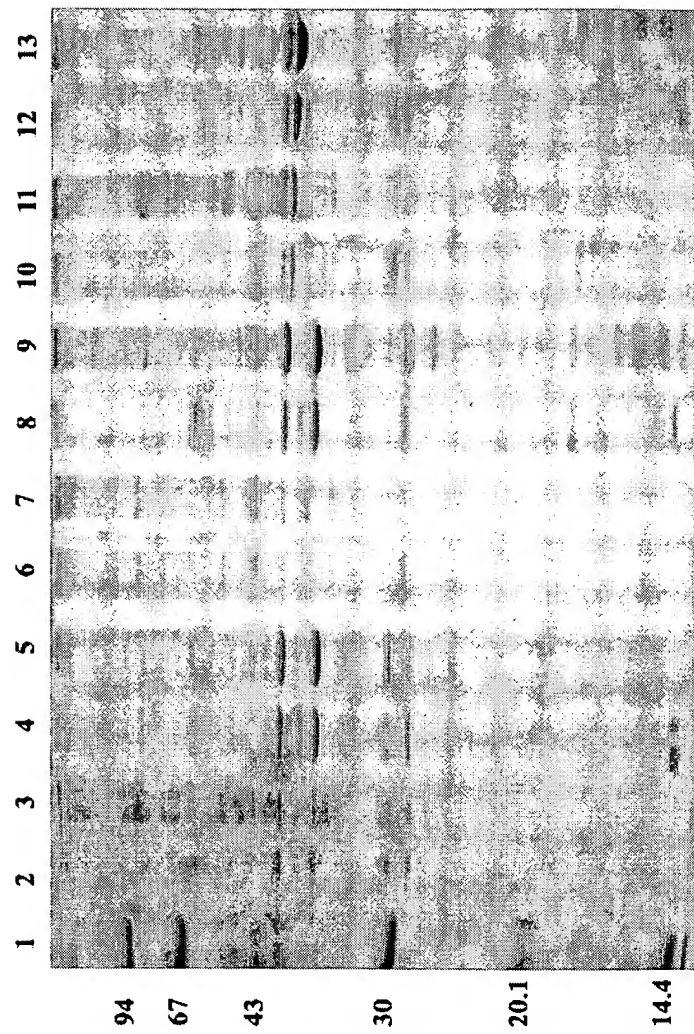


FIG. 2

FIG. 3.

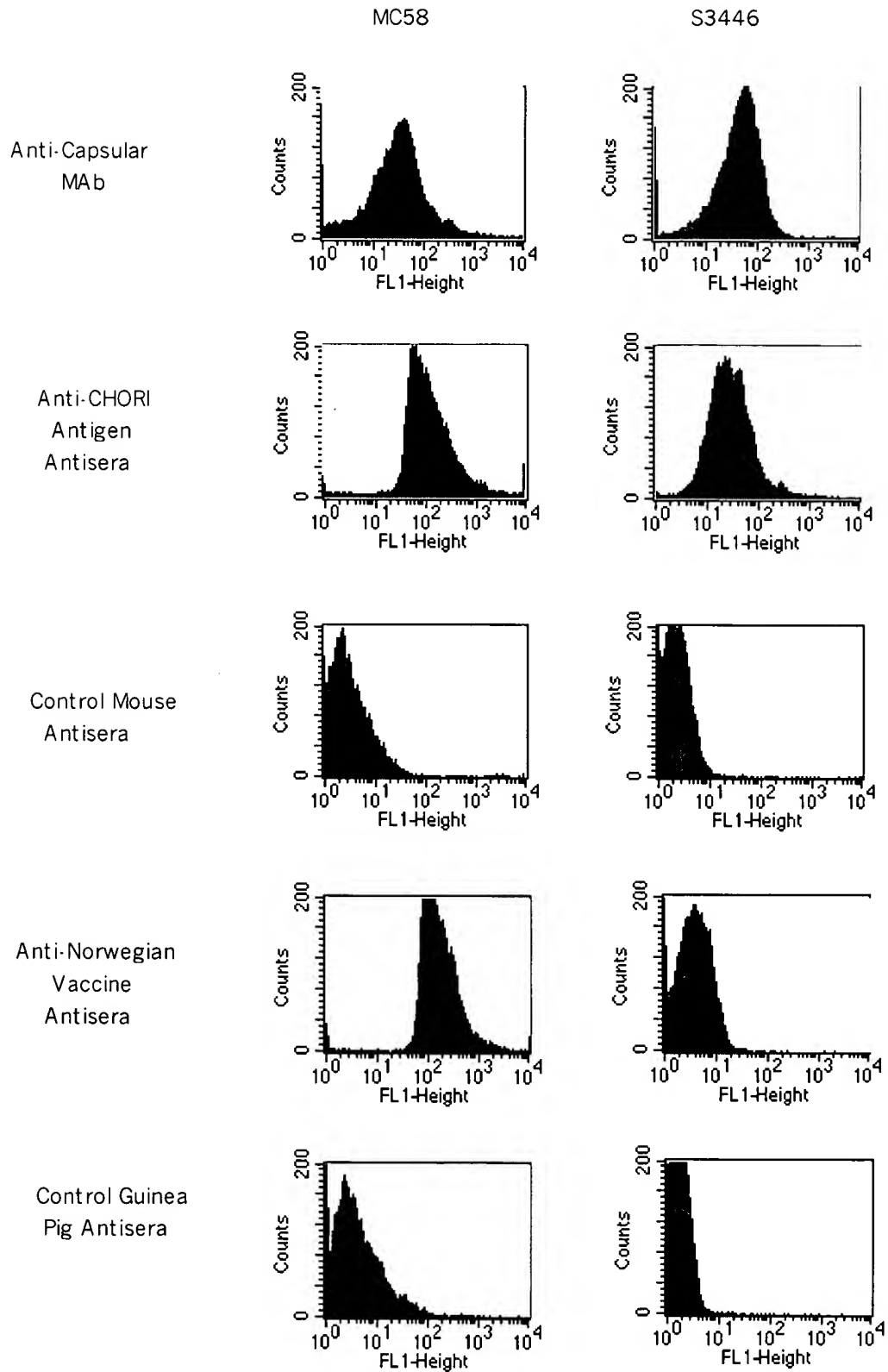


FIG. 4. Bacterial cell surface binding of antisera determined by indirect fluorescence flow cytometry

| Strain (serosubtype) | PorA heterologous to CHORI vaccine strains ⁺⁺⁺ | Surface reactivity by indirect fluorescence flow cytometry (1/titer)+ | | |
|-------------------------|--|--|---------------------------|-------------------------|
| | | Anti-CHORI ⁺⁺ | Anti-Norway ⁺⁺ | Anti-NspA ⁺⁺ |
| 1000 (5) | - | >200 | >200 | 20 |
| 2996 (5,2) | - | 2000 | <20 | 20 |
| 8047 (5,2) | - | >200 | <20 | >20 |
| BZ198 (4) | - | 2000 | 200 | >20 |
| CU385 (19,15) | + | >200 | <20 | >20 |
| IH5341 (7,16) | + | >200 | >200 | <20 |
| M136 (P-) | + | <20 | <20 | <20 |
| M986 (5,2) | - | 2000 | <20 | <20 |
| MC58 (7,16) | + | 200 | >200 | <20 |
| NG3/88 (1) | + | 200 | 200 | <20 |
| NMB (.5,2) | - | 2000 | ND | >20 |
| S3446 (23,14) | + | 200 | <20 | <20 |

+Titer is defined as the dilution required to give 50% of fluorescence (FL1-Height) of 10 or greater over background fluorescence of cells in the presence of control sera.

++Anti-CHORI antisera prepared in mice by sequential immunization with MV from strain RM1090 (C:2a;P1.5,2), then with MV from strain BZ198 (B:NT:P1.4) followed by OMV from strain Z1092 (A:4,21;P1.10) (see text). Anti-Norway refers to antiserum from guinea pigs given two injections of OMV vaccine prepared from strain H44/76 (B:15:P1.7,16) by the National Institute of Public Health ("MenB-Folkehelsa"), Oslo, Norway. Anti-NspA refers to antisera prepared in CD1 mice given three injections of recombinant NspA as described by Moe et al. (1999 Infect. Immun. 67: 5664).

+++Serosubtype (PorA) differs from those of the three strains used to prepare the vaccine. (see FIG. 21 and 22).

FIG. 5. Reactivity of CHORI antisera against *N. meningitidis* serogroup A and C strains

| Strain (serogroup:serosubtype) | Bactericidal Activity (1/titer)* | | Surface binding by indirect fluorescence flow cytometry (1/titer) ⁺ | |
|-----------------------------------|-------------------------------------|----------------|--|----------------|
| | Negative control sera | Anti- CHORI | Negative control sera | Anti- CHORI |
| 60E (C:P1.7,1) | <10 | >250 | <20 | ~2000 |
| Z1073 (A:P1.3,6) | <10 | >250 | ND | >>100 |

*Dilution of serum yielding 50% decrease in colony forming units (CFU) per ml after 60 minutes incubation of bacteria in the presence of human complement as compared to CFU/ml at time zero of controls (see FIG. 6 below).

+See footnotes to FIG. 4 and text

FIG. 6. Results of a bactericidal assay testing anti-CHORI antigen, anti-rNspA, and anti-Norwegian vaccine antisera against meningococcal B strain 2996

| Complement | Animal source of sera or mAb | Antibody/Antisera ⁺ | Final Concentration /Dilution | CFU/20 µl 0' | CFU/20 µl 60' | % Survival |
|------------|------------------------------|--------------------------------|-------------------------------|--------------|---------------|------------|
| None | - | None | 0 | 189 | 250 | 132 |
| None | - | None | 0 | 171 | 250 | 146 |
| Active | - | None | 0 | 175 | 250 | 143 |
| Inactive | - | None | 0 | 180 | 250 | 139 |
| Active | - | Complement | 1:5 | 190 | 250 | 132 |
| Active | Mouse | Anti-capsular mAb | 200µg/ml | | 1 | 1 |
| Active | Mouse | Anti-capsular mAb | 100µg/ml | | 43 | 24 |
| Active | Mouse | Anti-capsular mAb | 50µg/ml | | 225 | 124 |
| Inactive | Mouse | Anti-capsular mAb | 200µg/ml | | 230 | 127 |
| Active | Mouse | Anti-rNspA | 1:10 | | 250 | 138 |
| Active | Mouse | Anti-rNspA | 1:50 | | 250 | 138 |
| Active | Mouse | Anti-rNspA | 1:250 | | 250 | 138 |
| Active | Mouse | Anti-CHORI antigen | 1:10 | | 0 | 0 |
| Active | Mouse | Anti-CHORI antigen | 1:50 | | 2 | 1 |
| Active | Mouse | Anti-CHORI antigen | 1:250 | | 55 | 30 |
| Active | Mouse | Anti-E. coli control | 1:10 | | >250 | 138 |
| Active | Guinea pig | Anti-Norwegian vaccine | 1:5 | | 220 | 122 |
| Active | Guinea pig | Anti-Norwegian vaccine | 1:25 | | 245 | 135 |
| Active | Guinea pig | Anti-Norwegian vaccine | 1:125 | | 250 | 138 |
| Active | Guinea pig | Anti-alum control | 1:5 | | 250 | 138 |

⁺See footnotes to FIG. 4 and text

FIG. 7. Complement-mediated bactericidal activity of antisera and antibodies.

| Strain (serosubtype) | PorA heterologous to CHORI vaccine strains | Bactericidal activity (1/titer) ⁺ | | | |
|----------------------|--|--|-----------------|-----------|--|
| | | Anti-CHORI | Anti-Norway | Anti-NspA | |
| 1000 (5) | - | 130 | >125 | <10 | |
| 2996 (5,2) | - | >250 | <5 | <10 | |
| 8047 (5,2) | - | >250 | <5 | <10 | |
| BZ198 (4) | - | >250 | I ⁺⁺ | 110 | |
| CU385 (19,15) | + | >250 | <25 | <10 | |
| IH5341 (7,16) | + | >250 | I ⁺⁺ | <10 | |
| M136 (P-) | + | <10 | <5 | <10 | |
| M986 (5,2) | - | >250 | <5 | <10 | |
| MC58 (7,16) | + | >250 | >125 | <10 | |
| NG3/88 (1) | + | 13 | 9 | <10 | |
| NMB (5,2) | - | >100 | <5 | 16 | |
| S3446 (23,14) | + | 10 | <5 | <10 | |

+See footnotes to FIGS. 4 and 5 and text. Titer > refers to highest dilution tested; titer < refers to lowest dilution tested
 ++I, indeterminate due to the presence of bactericidal activity in the negative control antisera against this strain.

FIG. 8. Complement-mediated bactericidal activity of antisera from mice immunized with the indicated vaccines.

| Strain (serosubtype) | PorA heterologous to CHORI vaccine strains ⁺⁺⁺ | Bactericidal activity (1/titer) ⁺⁺⁺ | | | |
|-------------------------|---|--|--|---|---|
| | | CHORI CFA ⁺ (N=7) | CHORI/ Al ₂ (OPO ₄) ₃ ⁺ (N=7) | CHORI MIX/ Al ₂ (OPO ₄) ₃ ⁺ (N=10) | E. COLI MV/ Al ₂ (OPO ₄) ₃ (N=10) |
| 1000 (5) | - | 20 | 128 | 6 | <4 |
| 8047 (5,2) | - | 125 | 300 | 125 | <25 |
| BZ198 (4) | - | 650 | 220 | 1000 | <4 |
| BZ198 NspA (4) | - | 317 | 131 | 235 | <4 |
| BZ83 (10) | - | 275 | 109 | 205 | <25 |
| CU385 (19,15)++ | + | >128 | 128 | <4 | <5 |
| H44/76 (7,16) | + | >128 | >128 | 21 | 6 |
| M136 (P-) | + | 100 | <4 | 5 | <4 |
| M986 (5,2) | - | 193 | 101 | 133 | <4 |
| MC58 (7,16)++ | + | 47 | 8 | 7 | <4 |
| NG3/88 (7,1) | + | <4 | 4 | <4 | <4 |
| NGP165 (5,2) | - | 82 | 120 | 90 | <4 |
| NMB (5,2) | - | 183 | 441 | 141 | <4 |
| S3032 (12,16) | + | 125 | 400 | 230 | <25 |
| S3446 (22,14) | + | 18 | <4 | <4 | <4 |

+CHORI/CFA, sequential immunization with a 5 µg dose of strain RM1090 (C:2a;P1.5,2) MV with CFA, strain BZ198 (B:NT:P1.4) MV with IFA, and strain Z1092 OMV (A:4,21:P1.10) without adjuvant; CHORI/Al₂(OPO₄)₃ same as CHORI/CFA except using aluminum phosphate as an adjuvant; CHORI MIX/Al₂(OPO₄)₃ same as CHORI/Al₂(OPO₄)₃ except each 5 µg dose contained an equal mixture of the three MV/OMV preparations; E. COLI MV/Al₂(OPO₄)₃ MV prepared from E. coli strain BL21(DE3).
⁺⁺w/glu, cell culture grown in the presence of 0.3% glucose. ⁺⁺⁺See footnotes and text of FIG. 4.

FIG. 9. Bactericidal activity of antisera from guinea pigs immunized with the indicated vaccines⁺.

| Strain (serosubtype) ⁺⁺ | PorA heterologous to CHORI vaccine strains ⁺⁺⁺ | Bactericidal activity (1/titer) ⁺⁺⁺ | | |
|---------------------------------------|---|---|------------------------------------|--|
| | | CHORI/Al ₂ (OPO ₄) ₃ (N=8) | CHORI/Al(OH) ₃ (N=3) | E. COLI MV/Al ₂ (OPO ₄) ₃ (N=6) |
| M136 (P-) | + | <4 | <4 | <4 |
| S3446 (22,14) | + | 6 | 4 | <4 |
| CU385 (19,15) | + | 12 | 5 | <4 |
| 1000 (5) | - | 64 | 16 | <4 |
| H44/76 (7,16) | + | 64 | 16 | <4 |
| BZ83 (10) | - | 24 | 12 | <4 |
| 8047 (5,2) | - | >128 | 100 | <4 |
| BZ198 (4) | - | 28 | 6 | <4 |
| BZ198Δ _{spA} (4) | - | 19 | 5 | <4 |
| NG3/88 (7,1) ⁺⁺ | + | 9 | 5 | <4 |

⁺CHORI/Al₂(OPO₄)₃, sequential immunization with a 5 microgram dose of strain RM1090 (C:2a;P1.5,2) MV, strain BZ198 (B:NT:P1.4) MV, and strain Z1092 OMV (A:4,21:P1.10) aluminum phosphate as an adjuvant; CHORI/Al(OH)₃, same as CHORI/Al₂(OPO₄)₃ except using aluminum hydroxide as an adjuvant; E. COLI MV/ Al₂(OPO₄)₃, MV prepared from E. coli strain BL21(DE3).

⁺⁺All strains were grown in the presence of 0.3% glucose except for strains M136 and NG3/88.

⁺⁺⁺See footnotes and text of FIG. 4.

FIG. 10. Passive protection in infant rats against meningococcal B strain 8047 bacteremia by antisera and antibodies.+

| Treatment ⁺⁺ | Dose/rat or Serum Dilution (100 microliters) | Blood Culture Obtained at 18 hrs | |
|-------------------------|--|----------------------------------|-----------------------------------|
| | | No. Positive/total no. | Geo. Mean, 10 ³ CFU/ml |
| Anti-Capsular mAb | 10 micrograms | 0/5 | <1 |
| PBS control | - | 5/5 | >200 |
| Anti-E. coli control | 1:20 | 5/5 | >200 |
| Anti-CHORI | 1:20 | 0/5 | <1 |
| Anti-Norway | 1:20 | 5/5 | 83 |
| Alum control | 1:20 | 5/5 | 178 |

+Animals were pretreated at time 0 with control or test antibodies and challenged 2 hours later with 5×10^3 colony forming units of log phase N.meningitidis strain 8047 given IP.

++See footnotes to FIG. 4 and text.

FIG. 11. Passive protection in infant rats against meningococcal B strain 8047 bacteremia by guinea pig antisera.

| Treatment [†] | Dose/rat or Serum Dilution (100 microliters) | Blood Culture Obtained at 18 hrs | |
|--|--|----------------------------------|--------------------------------------|
| | | No. Positive/total no. | Geo. Mean, 10 ³ CFU/ml |
| Pre-immunization | 1:10 | 6/6 | 21.9 |
| Anti-CHOR/ Al ₂ (OPO ₄) ₃ | 1:10 | 0/6 | <0.001 |
| Anti-CHOR/ Al ₂ (OPO ₄) ₃ | 1:100 | 4/6 | 1.3 |
| Anti-CHOR/ Al ₂ (OPO ₄) ₃ | 1:1000 | 6/6 | 193 |
| Anti- CHOR/Al(OH) ₃ | 1:10 | 0/6 | <0.001 |
| Anti- CHOR/Al(OH) ₃ | 1:100 | 6/6 | 47.4 |
| Anti- CHOR/Al(OH) ₃ | 1:1000 | 6/6 | 32.0 |
| Anti-E. coli MV | 1:10 | 6/6 | 110 |
| Mouse anti-capsular mAb (SEAM 3) | 20 µg | 3/3 | 1.4 |

[†]See footnotes to FIGS. 9 and 10 and text.

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T02220"2222T000

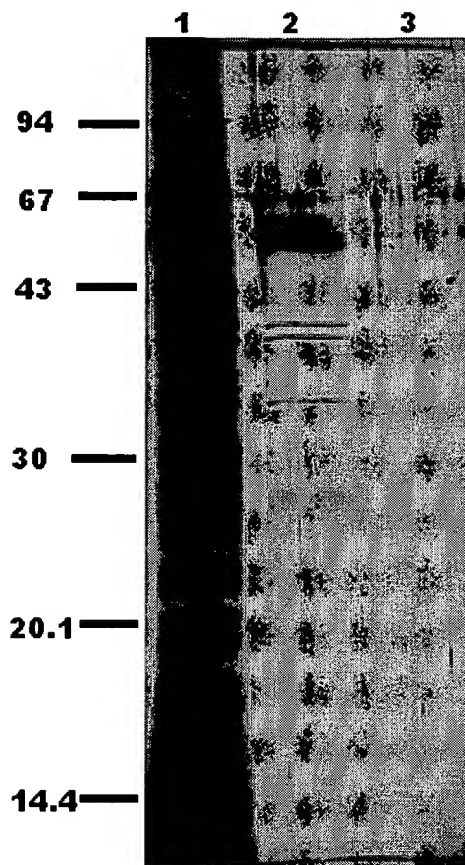


FIG. 12.

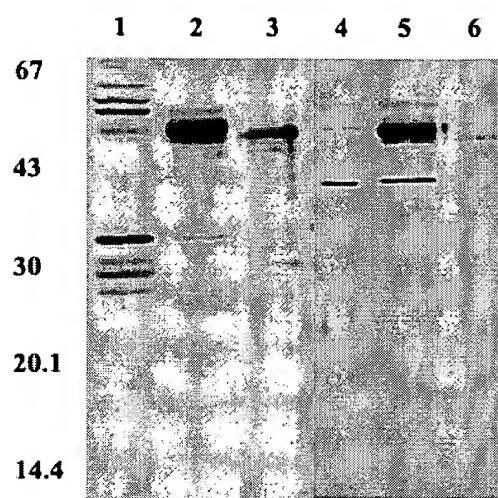


FIG. 13

FIG. 14. Bacterial surface accessible proteins precipitated by pooled antisera from mice sequentially immunized with MenC strain RM1090 MV, MenB strain BZ198 MV, and MenA strain Z1092 OMV.

| Strain/Sample | Serotype:subtype ⁺ | Precipitated Proteins (by apparent mass in kDa) | | |
|---------------|-------------------------------|---|------------------|------|
| | | 37-41 | 31-33 | <30 |
| RM1090MV | 2a:P1.5,2:L3,7 | 40.7, 39.6 | 32 | |
| BZ198 MV | NT:NST | 37.1, 35.1 | 32,30 | |
| Z1092 OMV | 4,21:P1.10 | 40.7, 39.1, 38.6, 37.6 | 33.1, 32.5, 31.5 | |
| BZ198 | NT:NST | | 32.5 | 14.5 |
| CU385 | 4,7:P1.19,15 | | 32.4 | |
| MC58 | 15:P1.7,16 | | 32.9 | |
| NG3/88 | 8:P1.1 | | 32.9 | 25.7 |
| NMB | 2b:P1.5,2 | 40.7, 39.6 | 33 | 14.5 |
| S3446 | 19,14:P1.23,14 | | 32.9 | 25.7 |

⁺See text and footnotes of Tables 21 and 22 (below)

FIG. 14A Bacterial surface accessible proteins precipitated by pooled antisera from mice sequentially immunized with MenC strain RM1090 MV, MenB strain BZ198 MV, and MenA strain Z1092 OMV.

| Strain | Serotype:subtype + | Precipitated Proteins (by apparent mass in kDa) | | | | | | | |
|--------|-----------------------|---|-----------|----------|-----------|-----------|-----------|--------|--------|
| | | >45 | | 36-45 | | 25-35 | | <25 | |
| | | Expt 1 | Expt 2 | Expt 1 | Expt 2 | Expt 1 | Expt 2 | Expt 1 | Expt 2 |
| BZ198 | NT:NST | 80 | | 36,39,43 | 37,40 | 28,30 | 28 | 14.5 | 12 |
| CU385 | 4,7:P1.19,15 | 80 | | 38,42 | 42 | 30,34 | | 10 | 11 |
| 1000 | NT:P1.5 | | ND | 41,45 | ND | 26 | ND | | ND |

+See text and footnotes of FIGS. 21 and 22 (below). Expts 1 and 2 refer to experiments performed with immune serum pools from different groups of mice immunized with different CHORI vaccine preparations. ND= not done (strain 1000 tested with immune serum from one group of immunized mice).

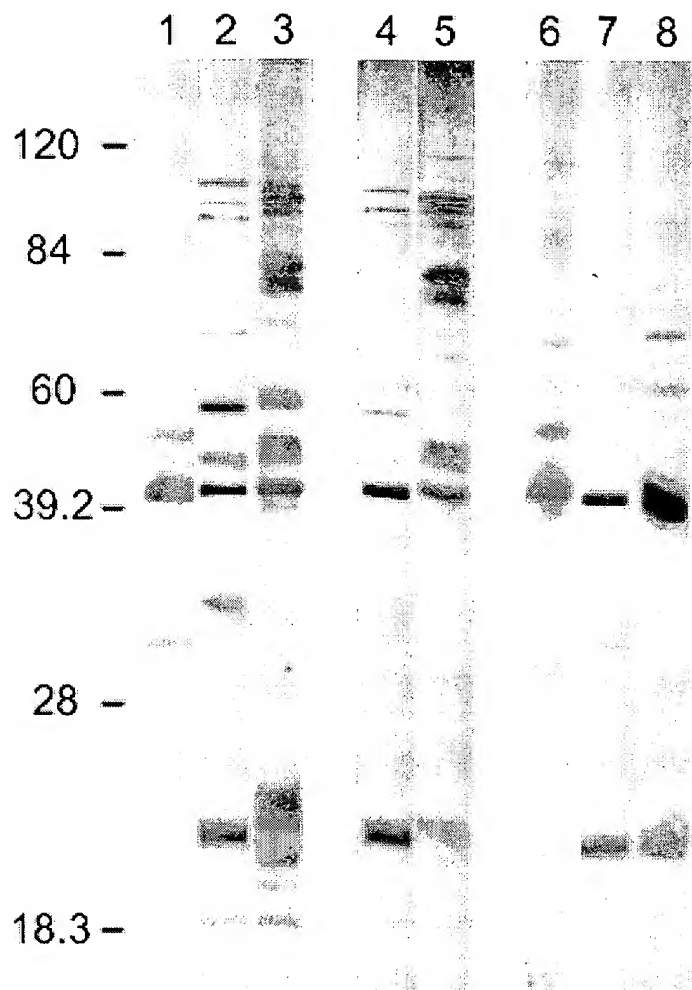


FIG. 15

FIG. 16. Proteins reactive with anti-CHORI antigen antisera by Western blot of MV and OMV preparations

| Mouse anti-CHORI/CFA antisera ⁺ | | Mouse anti-CHORI A1 ₂ (OPO ₃) ₂ ⁺ | | Guinea pig anti-CHORI/A1 ₂ (OPO ₃) ₂ antisera ⁺⁺ | |
|--|----------|--|----------|---|-----------|
| RM1090 MV | BZ198 MV | Z1092 OMV | BZ198 MV | RM1090 MV | Z1092 OMV |
| | 119 | | | | |
| 108 | | | | | |
| 101 | | 101 | 101 | | |
| | 96 | 97 | 95 | | |
| | 93 | 93 | 91 | | 92 |
| | | 88 | | | |
| | | 81 | | | |
| | | 76 | | | |
| 67 | 67 | 69 | | 66 | 76 |
| | | | | 62 | 68 |
| 53* | 56* | 57* | 56 | 53 | 64 |
| | 50 | 50 | | 55 | 59 |
| 46* | 47* | 47* | 47 | 47 | |
| | 36 | 38 | | 46 | 46 |
| 33* | 33* | 35* | 33 | 34 | |
| | 27 | | | 32 | 33 |
| | 20* | 21* | 20 | 24 | |
| | | 19 | | 20 | |
| | | 18* | 18 | 19 | 19 |
| | 18* | 18* | 18 | | |

⁺See footnote and text of FIG. 8.

⁺⁺See footnote and text of FIG. 9.

*Indicates proteins most reactive with CHORI/CFA antisera and common to at least two of the three vaccine preparations.

FIG. 17. Reactivity of anti-CHORI antisera with LOS by ELISA

| Antisera ⁺ | RM1090 LOS (1/titer) ⁺⁺ | | BZ198 LOS (1/titer) ⁺⁺ | | Z1092 LOS (1/titer) ⁺⁺ | |
|--|------------------------------------|-------------------------|-----------------------------------|-------------------------|-----------------------------------|-------------------------|
| | Unabsorbed | Absorbed ⁺⁺⁺ | Unabsorbed | Absorbed ⁺⁺⁺ | Unabsorbed | Absorbed ⁺⁺⁺ |
| Mouse anti-CHORI | <100 | <100 | 900 | <100 | 150 | <100 |
| Mouse anti-CHORI mix | 900 | 100 | 200 | <100 | 600 | 100 |
| Guinea pig anti-CHORI | <100 | <100 | 350 | 100 | <100 | <100 |
| Guinea pig anti-CHORI mix ⁺⁺⁺ | <100 | <100 | 300 | 100 | <100 | <100 |

+ See footnotes and text of FIG. 8 and 9.

⁺⁺Titer is defined as the dilution of serum giving an OD 405 nm of 0.5 after 1 hr incubation with substrate.

⁺⁺⁺Same as used to prepare mouse anti-CHORI antisera mix (see FIG. 8) except that total dose of 25 micrograms protein was given rather than 5 micrograms.

⁺⁺⁺⁺After incubation with LOS-BSA coupled to Sepharose (see text).

FIG. 18. Bactericidal activity of anti-CHORI antisera before and after absorption of anti-LOS antibodies.

| Serum ⁺⁺⁺ | Strain BZ198 (1/titer) ⁺ | | Strain S3032 (1/titer) ⁺ | |
|---------------------------|-------------------------------------|------------------------|-------------------------------------|------------------------|
| | Unabsorbed | Absorbed ⁺⁺ | Unabsorbed | Absorbed ⁺⁺ |
| Mouse anti-CHORI | 49 | 28 | 259 | 247 |
| Mouse anti-CHORI MIX | 350 | 111 | 234 | 102 |
| Guinea pig anti- CHORI | 125 | 93 | 13 | 5 |
| Guinea pig mix | 77 | 31 | <5 | 14 |

⁺See footnote and text to FIG. 5.

⁺⁺After incubation with LOS-BSA coupled to Sepharose (see text).

⁺⁺⁺See footnote and text to FIG. 17

FIG. 19. Reactivity of mAbs produced by immunization with CHORI vaccine with bacterial strains, LOS, and rNspA by ELISA.

| Strain+ | [mAb] (ng/ml) giving OD 405 nm = 0.5 after 1 hr incubation with substrate | | | | |
|----------------|---|--------------------|---------------|---------------------|--|
| | 1D9 (IgG2a) | 4B11 (IgM) | 9B8 (IgG3) | 14C7 (IgG3) | Anti-NspA mAb AL4 ⁺⁺⁺ (IgG2a) |
| Nm 1000 | 500 | >720 ⁺⁺ | >3970 | 7380 ⁺ | 1000 |
| Nm 4335 | 500 | >720 | 13 | 30 | 30 |
| Nm 8047 | 200 | 2.4 | >3970 | 10 | 20 |
| Nm 8047ΔNspA | 600 | >720 | >3970 | >7380 | >5400 |
| Nm BZ198 | 600 | >720 | 16 | 2 | 20 |
| Nm BZ198 ΔNspA | 600 | >720 | 16 | >7380 | >5400 |
| Nm BZ83 | 600 | >720 | >3970 | 273 | 80 |
| Nm CU385 | 600 | >720 ⁺⁺ | >3970 | >7380 ⁺⁺ | 180 |
| Nm M136 | 600 | >720 | >3970 | 36 | 400 |
| Nm M3966 | 1000 | >720 | >3970 | 0.5 | 50 |
| Nm M986 | 800 | >720 | >3970 | 5 | 400 |
| Nm NG3/88 | 600 | 0.8 | >3970 | 1 | 70 |
| Nm NGE31 | 500 | >720 | >3970 | 5 | 100 |
| Nm NGF26 | 600 | 2.4 | >3970 | 0.4 | 40 |
| Nm S3446 | 500 | >720 | >3970 | 0.2 | 40 |
| Hi Minn A | >8300 | >720 | >3970 | >7380 | ND |
| Hi Eagan | >8300 | >720 | >3970 | >7380 | ND |
| Nm RM1090 LOS | >8300 | >720 | >3970 | >7380 | ND |
| Nm BZ198 LOS | >8300 | >720 | >3970 | >7380 | ND |
| Nm Z1092 LOS | >8300 | >720 | >3970 | >7380 | ND |
| rNspA MV | >8300 | >720 | >3970 | 28 | 6 |

⁺Nm, *Neisseria meningitidis*; Hi, *Haemophilus influenzae*

⁺⁺Although negative by ELISA, 14C7 is bactericidal for these strains (see FIG. 20).

⁺⁺⁺ See Moe et al. Infect Immun. 2001 69:3762)

FIG. 20. Bactericidal activity of mAbs produced by immunization with CHORI vaccine.

| Strain (serosubtype) | PorA heterologous to CHORI vaccine strains ⁺ | mAb tested for bactericidal activity ⁺⁺ | | | | |
|-------------------------|---|--|--------|-----|--------|-------------------------|
| | | 1D9 | 4B11 | 9B8 | 14C7 | AL12 ⁺⁺ + |
| 1000 | - | - | + | - | + | + |
| BZ198 | - | - | static | + | + | + |
| BZ198ΔN spA | - | - | - | + | - | - |
| CU385 | + | - | + | - | + | - |
| M986 | - | - | - | - | + | - |
| NG3/88 | + | - | static | - | static | - |

⁺See text and footnotes of FIG. 4.

⁺⁺ + refers to bactericidal when tested at less than or equal to 100 micrograms/ml; static refers to a percent survival of CFU/ml at 60 min is greater than 50% but less than 100% (see FIG. 6)

⁺⁺⁺ Moe et al. Infect Immun. 2001 69:3762

FIG. 21. Meningococcal serotype and serosubtype defining monoclonal antibodies available from RIVM*

| Serotyping reagents | | | Serosubtyping reagents | | |
|---------------------|------|-----|------------------------|--------|-----|
| Monoclonal | Type | Ig | Monoclonal | Type | Ig |
| MN3C6B | 1 | G2b | MN14C2.3 | P1.1 | G2a |
| MN2D3F | 2A | G2a | MN16C13F4 | P1.2 | G2a |
| MN2C3B | 2B | G2a | MN20B9.34 | P1.4 | G2a |
| MN14G21 | 4D | G2a | MN22A9.19 | P1.1.5 | G2a |
| MN5C8C | 14 | G2a | MN19D6.13 | P1.6 | G3 |
| MN15A14H6 | 15 | G2a | MN14C11.6 | P1.7 | G2a |
| | | | MN5A10F | P1.9 | G2a |
| | | | MN5A10F | P1.9 | G2a |
| | | | MN20F4.17 | P1.10 | G2b |
| | | | MN20A7.10 | P1.12 | G3 |
| | | | MN24H10.75 | P1.13 | G2a |
| | | | MN21G3.17 | P1.14 | G3 |
| | | | MN3C5C | P1.15 | G3 |
| | | | MN5C11G | P1.16 | G2b |

*Rijksinstituut Voor Volksgezondheid en Milieu (RIVM), P.O. Box 457, 3720 AL Bilthoven, The Netherlands (reference *FEMS Microbiology Letters* **48** (1987) 367-371).

FIG. 22. Serogroup, serotype, and serosubtype defining monoclonal antibodies available from NIBSC*

| Serogroup | Cat. No. | Serotype | Cat. No. | Serosubtype | Cat. No. |
|-----------|----------|----------|----------|-------------|----------|
| A | 95/674 | P2.2a | 95/682 | P1.1 | 95/694 |
| B | 95/750 | P2.2b | 95/684 | P1.10 | 95/710 |
| C | 95/678 | P3.1 | 95/680 | P1.12 | 95/712 |
| | | P3.14 | 95/688 | P1.13 | 95/714 |
| | | P3.15 | 95/690 | P1.14 | 95/716 |
| | | P3.21 | 95/692 | P1.15 | 95/718 |
| | | P3.4 | 95/686 | P1.16 | 95/720 |
| | | | | P1.2 | 95/696 |
| | | | | P1.3 | 95/698 |
| | | | | P1.4 | 95/700 |
| | | | | P1.5 | 95/702 |
| | | | | P1.6 | 95/704 |
| | | | | P1.7 | 95/706 |
| | | | | P1.9 | 95/708 |

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